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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/389,565	09/03/1999	DAVID M. NEVILLE, JR.	14028.0290	5574

7590 06/13/2002

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	27

DATE MAILED: 06/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.	Applicant(s)
09/389,565	Neville et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *May 20, 2002* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see NOTE below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____

3. ☐ Applicant's reply has overcome the following rejection(s):

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
   See attachment

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *none*

   Claim(s) objected to: *none*

   Claim(s) rejected: *30-33 and 37-42*

   Claim(s) withdrawn from consideration: _____

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☒ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). *23* .

10. ☐ Other:

DETAILED ACTION

1. Applicant's After Final Amendment and the 1.132 Declaration of Inventor David M. Neville, filed 5/20/02 are acknowledged. Said amendment and declarations have been entered and considered.

2. Applicant arguments, filed 5/20/02, have been fully considered but are not found persuasive. Applicant argues that "DT390 is not claimed in the present invention." The Examiner apologizes for any confusion caused by the imprecise language used, the Examiner intended that the rejection be based on an invention comprising DT390. Applicant argues that the declaration of Inventor Neville provides data indicating the unpredictability of the claimed invention. Said declaration, and the accompanying references have been fully considered.

Inventor Neville argues that, "A fusion immunotoxin constructed of the first 390 residues of diphtheria toxin followed by the sFv of the anti-CD3ε antibody of UCHT1 has surprising and unexpected properties," and "These surprising and unexpected properties arise from characteristics of the sFv moiety of UCHT1 that are not present in most other sFv constructs of other anti-CD3 antibodies and also arise from the unique synergy between DT390 and the CD3ε epitope." First note that it is clear the declaration is not intended as support for Claim 30 which recites a generic DT construct. In paragraph 2, the inventor indicates that he has produced three additional anti-CD3 sFvs. In paragraph 3, the inventor states that the additional anti-CD3 sFvs "showed a 2-3 log loss of potency when compared to DT390sFv or DT389sFv of UCHT1," while maintaining "approximately the same affinity when assayed by FACS analysis on monkey or human T cells expressing CD3." The Inventor then draws the conclusion that "These data suggest that the non-predictable features lie in the variable sFv properties of UCHT1." In paragraphs 4-6 the inventor discusses work from his laboratory published by Ma et al (1997) and Thompson et al (2001).

When considering the probative value of a 1.132 declaration the Examiner must consider several factors. Included in those factors are the nature of the matter sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion (MPEP 716.01(c)). Regarding the nature of the matter sought to be established, the inventor has stated that the instant invention comprises "surprising and unexpected properties," thus, a certain amount of

evidence demonstrating said "surprising and unexpected properties" would be required. Regarding the interest of the expert in the outcome of the case, clearly the inventor has a decided interest in the outcome on the determination of patentability of his own invention. Regarding the presence or absence of factual support for the expert's opinion, it appears that the only actual factual support for the instant invention are the inventor's assertions of paragraph 3 that his invention works better that comparable inventions. After a careful review of the Ma et al and Thompson et al papers, discussed in paragraphs 4-6, it is the Examiner's position that the references at best, are neutral regarding the instant invention, and at worst, actually teach away from the invention. Both references seem to teach that the best monovalent single chain immunotoxins are not particularly effective. Both references disclose new divalent immunotoxin constructs, and both references teach that the divalent immunotoxin is much preferred. Regarding the inventor's assertion that the immunotoxin of the instant claims "surprising and unexpected properties," the Examiner must also consider whether or not the evidence provided in the declaration comprises both statistical and practical significance, see MPEP 716.02(b). It is the Examiner's position that the inventor's assertions cannot be considered both statistically and practically significant, thus the assertions are insufficient to overcome the instant rejections.

3. Applicant is further advised that should the instant rejections over prior art be overcome, significant new considerations regarding the claims to methods of treatment would be required.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:00 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
June 7, 2002

Patrick J. Nolan, Ph.D.
Primary Examiner
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